Molecular basis of plasma membrane characteristics reflecting stem cell fate potential

Grant Award Details

Molecular basis of plasma membrane characteristics reflecting stem cell fate potential

Grant Type: Basic Biology V

Grant Number: RB5-07254

Project Objective: To test a hypothesis that unique membrane capacitance values of human neural progenitors (NPs) and astrocyte progenitors (APs) reflect distinct patterns of cell surface glycosylation, and these differences in glycosylation are sufficient to dictate cell fate by regulating specific profiles of cell surface receptors.

Investigator:

Name:	Lisa Flanagan
Institution:	University of California, Irvine
Type:	PI

Disease Focus: Neurological Disorders

Human Stem Cell Use: Adult Stem Cell

Award Value: $994,108

Status: Active

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Molecular basis of plasma membrane characteristics reflecting stem cell fate potential

Public Abstract: Stem cells generate mature, functional cells after proteins on the cell surface interact with cues from the environment encountered during development or after transplantation. Thus, these cell surface proteins are critical for directing transplanted stem cells to form appropriate cells to treat injury or disease. A key modification regulating cell surface proteins is glycosylation, which is the addition of sugars onto proteins and has not been well studied in neural stem cells. We focus on a major unsolved problem in the neural stem cell field: do different proteins coated with sugars on the surfaces of cells in this lineage (neuron precursors, NPs and astrocyte precursors, APs) determine what types of mature cells will form? We hypothesize key players directing cellular decisions are glycosylated proteins controlling how precursors respond to extracellular cues. We will address this hypothesis with aims investigating whether (1) glycosylation pathways predicted to affect cell surface proteins differ between NPs and APs, (2) glycosylated proteins on the surface of NPs and APs serve as instructive cues governing fate or merely mark their fate potential, and (3) glycosylation pathways regulate cell surface proteins likely to affect fate choice. By answering these questions we will better understand the formation of NPs and APs, which will improve the use of these cells to treat brain and spinal cord diseases and injuries.

Statement of Benefit to California: The goal of this project is to determine how cell surface proteins differ between cells in the neural lineage that form two types of final, mature cells (neurons and astrocytes) in the brain and spinal cord. In the course of these studies, we will uncover specific properties of human stem cells that are used to treat neurological diseases and injuries. We expect this knowledge will improve the use of these cells in transplants by enabling more control over what type of mature cell will be formed from transplanted cells. Also, cells that specifically generate either neurons or astrocytes can be used for drug testing, which will help to predict the effects of compounds on cells in the human brain. We hope our research will greatly improve identification, isolation, and utility of specific types of human neural stem cells for treatment of human conditions. Furthermore, this project will generate new jobs for high-skilled workers and, hopefully, intellectual property that will contribute to the economic growth of California.